REMARKS/ARGUMENTS

Claims 24-43 are active. These claims track and find support in the original claims and specification. Specific support may be located as follows: Claim 24 (Claim 1, page 6, lines 10 and 22), Claim 25 (Claim 8, page 3), Claims 26-27 (page 4, line 5), Claims 28-29 (page 11, lines 8-14, page 5, line 20 *ff.*), Claim 30 (page 11, lines 8-14), Claims 31-34 (page 6, lines 16-17), Claim 35 (page 6, line 13), Claim 36 (page 6, lines 26-27), Claim 37 (page 5, lines 26-28), Claim 38 (page 6, line 23), Claim 39 (Claims 1-3, page 6, line 6 *ff.*) and Claims 40-43 (Claims 2 and 4, page 6, lines 9-10, page 9, line 14). Accordingly, the Applicants do not believe that any new matter has been introduced.

The Applicants thank Examiners Shaw and Johannsen for the courtesies extended to them in the interview of March 9, 2007 and March 16, 2007. The basis for the restriction requirement was discussed. The Applicants requested that the Examiner extend examination to additional polymorphisms. The Examiner recommended that the claims be directed to the polymorphism at position 421 (the elected species), but agreed to reconsider the nature of the requirement, especially if other polymorphisms were claimed in combination with that at position 421. Ways to avoid the prior art were discussed. The Examiner indicated that Zamber was prior art under 35 U.S.C. 102(a) and could be avoided by perfecting the priority claim. The Examiner said that based on the date of June 1, 2002 indicated on the cover of Imai it had been applied under 35 U.S.C. 102(b).

Restriction/Lack of Unity

The Applicants previously elected with traverse, Group I, Claims 1-4, 8 and 20-21. An election of the SNP (single nucleotide polymorphism) at position 421 of SEQ ID NO: 1

was also made. Claims 5-7, 9-19 and 22-23 have been withdrawn from consideration and the Restriction/Lack of Unity Requirement made FINAL.

Objection—Claims

Claims 1-3 and 20 were objected to as encompassing non-elected subject matter. This objection is moot in view of the amendments above.

Rejection—35 U.S.C. §112, first paragraph

Claims 1-4, 8 and 20-21 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate description. This rejection is moot in view of the cancellation of these claims.

Rejection—35 U.S.C. §112, first paragraph

Claims 1-4, 8 and 20-21 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate enablement for the invention. This rejection is moot in view of the cancellation of these claims. It would not apply to the new claims because no undue experimentation would be required to make and use the invention. Even a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed", *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988).

"Any sample". One with skill in the art would have been able to select an appropriate biological sample without undue experimentation. Various routine assay techniques for determining polymorphisms in polynucleotides or amino acid substitutions in polypeptides are well-known in the art. New Claim 30 refers to specific types of samples exemplified in

the specification, although those of skill in the medical or biological arts would be able to select other appropriate samples.

"Any mammal". The Official Action asserts that the claimed method would not be useful for mammals in general, but only for humans. However, it provides no reasoning to substantiate this assertion. The initial burden is on the Office to establish a reasonable basis to question the enablement provided for the claimed invention, *In re Wright*, 27 USPQ2d 1510 (Fed. Cir. 1993), MPEP 2164.04. Furthermore, one with skill in the art would understand that the polymorphic genes may be expressed in non-human mammalian cells and exhibit their drug transport activity in such cells as disclosed on pages 28 and 29 of the specification.

"Any polymorphism". The new claims are directed to a polymorphism at position 421 of SEQ ID NO: 1.

"Any drug". The ABCG2 is a molecular pump which belongs to the ABC transporter superfamily, specification, page 10, lines 14-18. Based on this information, one with skill in the art would have been able to select an appropriate drug for use in conjunction with the claimed method, e.g., drugs on which such a molecular pump works. Moreover, based on the disclosure it would be a simple matter to determine whether or not a particular drug was affected by modification of the polypeptide of SEQ ID NO: 2 by merely comparing drug transport between the normal and mutated forms of this polypeptide.

The Applicants are not asserting that the claimed method will predict the ability of all drugs to be transported, only that it is within the skill of the art to apply the claimed method to various drugs without undue experimentation. In fact, the specification (Table 4, page 37), exemplifies drugs (Compound B) which are transported by ABCG2 as well as a drug (Camptothecin) which is not. Routine determination of appropriate drug types may be made by such a simple comparison. As held in *In re Wands*, a considerable amount of

experimentation is acceptable if it is merely routine, as it would be here. Furthermore, new Claims 25-27 are directed to specific types of drugs.

"Any cell transport". Some polymorphisms are associated with decreased drug transport or accumulation of drugs inside a cell (specification, page 5, lines 24-30) and other polymorphisms with decreased accumulation of drugs (page 4, lines 3-8). The specification enables the correlation of a particular polymorphism with relative increased or decreased drug transport capacity compared to given control cell line, e.g., SEQ ID NO: 1 is correlated with increased drug transport relative to other polymorphic forms of SEQ ID NO: 1. Similarly, these other polymorphs are correlated with relatively lower drug transport capacity than SEQ ID NO: 1. Nevertheless, new Claim 37 is specifically directed to correlating a polymorphism with decreased drug transport.

In regard to the *Wands* factors the Applicants note the following:

(A) the breadth of the claims has been substantially narrowed to a method involving a polymorphism at position 421 of SEQ ID NO: 1.

(B) the nature of the invention is not unpredictable since methods for determining drug transport capacity are well-known in the art, as are methods for correlating particular genes with this function. The claimed method steps are straightforward and well within the skill of those in the art.

(C) The state of the prior art shows that methods of detecting polymorphisms and determining drug transport capacity of cells are well-known.

(D) The level of ordinary skill in the molecular biological arts is high, generally Ph.D or post-doctoral level.

(E) The level of predictability in the art is high, based on the known functional activities of ABCG2 proteins, the simplicity of the method steps, and the exemplification of the method with classes of drugs like indolocarbazoles.

(F) and (G) The amount of direction in the specification is high and the claimed method is exemplified on pages 35-37 of the specification.

(H) The quantity of experimentation needed to make or use the invention is limited since the method only requires determining whether a mammalian cell has a polymorphism at position 421 of the ABCG2 gene or an amino acid substitution of SEQ ID NO: 2 and it would be routine to compare drug transport capacity of wild type (SEQ ID NO: 1 or 2) cells and cells containing a polymorphic variant of SEQ ID NO: 1 at position 421 (or at amino acid 141 of SEQ ID NO: 2).

Accordingly, the Applicants respectfully submit that this rejection would not apply to the present claims.

Rejection—35 U.S.C. §112, second paragraph

Claims 1-4, 8 and 20-21 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in view of the cancellation of these claims.

Rejection—35 U.S.C. §102(b)

Claims 1-4, 8 and 20-21 were rejected under 35 U.S.C. 102(b) as being anticipated by Imai et al., Mol. Canc. Ther. 1:611. This rejection is moot in view of the cancellation of these claims. It would not apply to the new claims since Imai was not published until June 18, 2002 (see publication date provided by Library of Congress Serials Database entry). While the date published on the cover of the journal is June 2, 2002, according to this database, the publication was not released to the public ("published") until June 18, 2002. On the attached Serials Database entry the first date (3Jul02) is the date the registration form was submitted, the second date (Jun02) is the date printed on the journal, and the third date (18Jun02) is the actual publication date of the issue.

The actual publication date of the issue was June 18, 2002, which is after the foreign priority date of this application and is less than one year prior to the U.S. filing date of this application. The Applicants provide herewith an English translation of their priority document which antedates Imai et al. Therefore, Imai is not prior art under either 35 U.S.C. 102(a) or (b).

Support for independent Claim 24 in the English translation of the priority document is indicated below:

> A method for predicting a drug transport capability of a mammalian cell (paragraph [0017] bridging pages 11-12, claim 1 on page 1), comprising:
>
> determining whether a mammalian cell has a polymorphism at position 421 of the ABCG2 gene of SEQ ID NO: 1 (page 12, [0018]), or
>
> determining whether an ABCG2 polypeptide produced by said mammalian cell has an amino acid substitution at position 141 of SEQ ID NO: 2 (page 12, [0019]);
>
> wherein the presence of a polynucleotide polymorphism at position 421 an amino acid substitution at position 141 is indicative of altered drug transport capability of said mammalian cell (page 22, [0043]).

Accordingly, this rejection would not apply to the present claims.

Rejection—35 U.S.C. §102(a)

Claims 1-4, 8 and 20-21 were rejected under 35 U.S.C. 102(a) as being anticipated by Zamber et al., Pharmacogenet. 13:19. This rejection is moot in view of the cancellation of these claims. It would not apply to the present claims, especially in view of the certified English translation of the priority document provided herewith which antedates this document.

Rejection—35 U.S.C. §103

Claims 21 was rejected under 35 U.S.C. 103(a) as being anticipated by Imai et al., Mol. Canc. Ther. 1:611, in view of Komatani et al., Canc. Res. This rejection is moot in view of the cancellation of Claim 21 and would not apply to the present claims for the reasons discussed above for Imai.

Rejection—35 U.S.C. §103

Claims 8 and 21 rejected under 35 U.S.C. 103(a) as being anticipated by Zamber et al., Pharmacogenet. 13:19, in view of Komatani et al., Canc. Res. This rejection is moot in view of the cancellation of Claims 8 and 21 and would not apply to the present claims for the reasons discussed above for Zamber.

Conclusion

In view of the above amendments and remarks, the Applicants respectfully submit that this application is in a condition for allowance. Early notification of such is earnestly requested.

Respectfully submitted,

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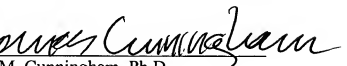

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